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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,035	06/23/2003	Mizuo Miyazaki	CPR-00101.P.1-US	9541

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KILYK & BOWERSOX, P.L.L.C.
400 HOLIDAY COURT
SUITE 102
WARRENTON, VA 20186

EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
11/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/602,035	MIYAZAKI, MIZUO	
	Examiner	Art Unit	
	MAURY AUDET	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/5/08*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/5/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's filing of the amendment (new claims 37-65), IDS and response are acknowledged.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The rejection of new claims 37-65 (virtual identical in scope to previous claims 1-32) under 35 U.S.C. 103(a) as being unpatentable over Powers et al. (US 5,543,396; also cited in IDS of 04/23/04, P5) in view of Porter et al. (US 5,591,199) and Scharpe et al. (US 2002/0061839 A1), is maintained for the reasons of record. Applicant's arguments have been considered but are not found persuasive.

Specifically, Applicant argues that surgical/tissue adhesion is distinct form adhesion resulting from inflammation/other biochemical pathways within the system. Yet, under the

broadest reasonably interpretation of surgical/tissue adhesion, inflammation is naturally a part of these processes as well, and thus part of those processes. Applicant argues on pages 7-8 that surgical/tissue adhesion as known in the art involves "fibrin bands". If this is a distinguishing pathway from how inflammation/other biochemical pathways cause 'adhesion', Applicant may wish to consider distinctly claiming (per support in the description) this 'fibrin band' connectivity v. how inflammatory connectivity of tissues results. In order to distinguish the overlapping adhesion processes.

The rejection is repeated below for continuity of record:

As also previously noted, Applicant's arguments were considered but were not found persuasive. Namely, as Applicant points out, Powers et al. teach that the elected peptide is used as "anti-coagulants, anti-inflammatory agents"; the latter being directed to the underlying physiological basis of tissue adhesion and reducing thereof, well known in the art to effectively carry out reducing adhesion formation (e.g. use of protease inhibitors in e.g. stents, see below "Prior Art Made of Record (on this point) and Not Relied On", citing by example Porter et al. (US 5,591,199)). The rejection as to the method and forms of administration thereto is maintained. In order to clarify the record, Porter et al. has been expressly incorporated in the rejection. The remainder of the rejection remains substantively unchanged, other than the express incorporation of Porter et al.

Powers et al. teach a pharmaceutical composition in any form (inherently containing a diluent or excipient since can be in the form of e.g. tablet, aqueous or oily suspension, etc.) (col. 16, lines 23-40), comprising the elected compound of the invention

Suc-Val-Pro-PheP(Oph)2 (e.g. Example 17), describes at the "best inhibitor for [serine proteases] chymotrypsin and chymotrysin-like enzymes" (col. 5, lines 40-44; col. 3, lines 50-53), which are involved in "tissue remodeling" [e.g. tissue adhesion formation] (col. 1, lines 41-43). However, Powers et al. does not expressly teach the use of Suc-Val-Pro-PheP(Oph)2 to reduce [tissue] adhesion formation (e.g. claim 1) or all the various forms of administration (e.g. claim 25-30, such as liposomes).

Porter et al. (US 5,591,199), also discussed previously under section "Prior Art Made of Record But Not Relied Upon" teach at col. 5-6 that protease inhibitors are known to be used for reducing aggregation/tissue adhesion, and applied via stents at the site of tissue for such ' purposes:

For restenosis inhibition, it is typically desirable to arrest the proliferation of smooth muscle cells. Accordingly, *drugs which prevent platelet aggregation and adhesion can be used, such as antiplatelets, antithrombogenics, and anticoagulants.* In addition, receptor blockers, growth factors and other hormones may be used to limit the normal repair response. The following are groups of particular drugs which can be used to treat vascular disease, such as atherosclerosis and restenosis: anticoagulants, including heparin, hirudin, hirulog, tissue plasminogen activator, and fibrinogen; anti-inflammatory agents, such as steroids, ibuprofen, aspirin, somatostatin, angiopeptin, and anti-inflammatory peptide 2; cytotoxins, including colchicine, dexamethasone, doxorubicin, methotrexate, and psoralen; antibiotics; and enzymes and enzyme inhibitors, including urokinase, 2,4-dinitrophenol, and thiol *protease inhibitor.*

Scharpe et al. teach the use of serine protease inhibitors such. as Suc-Val-Pro-Phe (para 69) in virtually any pharmaceutical admixture/formulation, such as liposomes (para 125).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the elected compound Suc-Val-Pro-PheP(Oph)2 to reduce [tissue] adhesion formation as

one of the methods relevant to inhibiting the actions of the serine protease chymotrypsin methods in Powers et al., because Powers et al. advantageously teaches the use of Suc-Val-Pro-PheP(Oph)2 to inhibit chymotrysin, which is a serine protease known to be used in the pathway of tissue remodeling (e.g. adhesion/aggregation/binding). One of ordinary skill in the art would recognize that administering Suc-Val-Pro-PheP(Oph)2 would combat such tissue adhesion caused by chymotrypsin based on the native properties therein, based on Powers et al. alone or in view of the analogous art teachings of Porter et al. that protease inhibitors are known to be used for reducing aggregation/tissue adhesion.

Additionally, it would have been obvious to one of ordinary skill in the art at the time of the invention to put the elected compound Suc-Val-Pro-PheP(Oph)2 in any formulation/ admixtures (e.g. liposomes) in the composition of Powers et al, because Scharpe et al. teach that like exact or like serine protease inhibitors may be put in composition with e.g. liposomes, etc. depending on the desired result/administration route; just as Powers et al. likewise discussed in terms of motivation for route/type of administration being left open to the skilled artisan and the desired effect. *Sharpe et al. is cited merely by example of art teaching/suggesting other known routes of administration of known compounds, since the art is well versed that administration routes/ranges are completely open to routine optimization, depending on the desired results/intended use, absent evidence to the contrary of some unexpected deleterious effect via one or more routes for the purpose intended.*

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at

the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg,* 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman,* 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum,* 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321 (d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-32 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 10/544,254 (Miyazaki et al., Publication US 2006/0122101 A1), is maintained for the reasons of record. Applicant argues '254 claims modes of administration via IV, oral, percutaneous that the present application does not claim. This is not found persuasive, as the present rejection is made

under obviousness, as such modes of administration are well known the ordinary skilled artisan and merely a matter of routine optimization, including guidance by the present specification, to which these claims are read in light thereof.

The remainder of the rejection is repeated below for continuity of record:

Although the conflicting claims are not identical, they are not patentably distinct from each other because even though the '254 expressly claims its subject matter in the form of a "medicament" only, therein, the limitations are directed to the presently elected compound Suc-Val-Pro-PheP(Oph)2 in any formulation/admixtures, for the purpose of inhibiting tissue adhesion.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Observations

As previously noted (Applicant's acknowledgement as well) claims 25-30 depend from claim 1 directly or indirectly, the first independent claim grouping, but are sandwiched in the middle of the second independent claim grouping (claim 16). It is suggested, for clarity (and along With any other amendments) that Applicant-consider amending the claims to delete claims **1-32** and start with new claims beginning at claim 25, wherein the claims are properly grouped.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications maybe obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, seehttp://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-91:97 (toll-free).

MA, 12/7/2007

/Andrew D Kosar/
Primary Examiner, Art Unit 1654